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Relationship between blood lead concentration and dietary intakes of infants from 3 to 12 months of age ☆

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Abstract

Data from a study of mother–infant pairs of low socioeconomic status living in Albany County, NY, were analyzed to determine the influence of diet and nutrition on the blood lead level of infants during the first year of life. Children's diets were assessed at 3-month intervals using a 24-h diet recall as reported by the primary caregiver. The potential impact of dietary consumption of protein, iron, zinc, calcium, vitamin D, and fat, as well as serum vitamin D and ferritin on blood lead levels at 6 and 12 months of age was examined with multivariable statistical analyses, controlling for other influences on lead levels. Neonates' blood lead levels were low at birth (geometric mean = 1.6 μg/dL), and none were elevated (⩾10 μg/dL). By 12 months, the mean blood lead for this sample was 5.1 μg/dL, and 18% of the sample had an elevated blood lead level. We observed significant inverse relationships between infants' 6-month lead level and their intake of zinc, iron, and calcium. At 12 months, low iron intake continued to be associated with higher lead levels, although zinc and calcium did not. Protein had a paradoxical effect, being associated with lower lead at 6 months, but higher lead at 12 months. Serum vitamin D and ferritin were not associated with lead levels, nor was vitamin supplement use. The results reported here emphasize the value of key minerals in the diet to reduce lead absorption during early infancy.

Keywords: Lead; Diet; Nutrition; Anthropometry; Children

1. Introduction

Lead is a heavy metal with no known benefit to the health of human beings. The effects of exposure to lead vary according to dose and the age of the exposed person (Agency for Toxic Substances and Diseases Registry, 1988). There is increasing evidence in children for adverse effects of lead at low levels of exposure, including decreased intelligence and reduced physical growth (Bornschein et al., 1985; Committee on Measuring Lead in Critical Populations, 1993; Dietrich et al., 1993; McMichael et al., 1988; Mushak et al., 1989; Needleman, 1983; Schwartz et al., 1986; Shukla et al., 1989) that may be present at lead levels below the CDC action level of 10 μg/dL (Canfield et al., 2003).

Exposure to lead begins before birth with its transference from the maternal circulation (Barltrop, 1969; Goyer, 1990) and increases rapidly in the first years of life as exposure to environmental lead increases (Bander et al., 1983).

Efforts to reduce lead levels and rates of lead poisoning in children are complicated by the pervasiveness of lead in the environment and the multiple sources and routes of exposure to lead. Although the average blood lead concentration among young children in the

☆ *Human subjects*: The research described in this article included human subjects and was conducted in accordance with national and institutional guidelines for the protection of human subjects. The Institutional Review Boards of the New York State Department of Health, Albany Medical Center (AMC), and the State University of New York at Albany reviewed and approved all data collection methods and procedures.

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United States has decreased markedly since 1980 (Brody et al., 1994; Mahaffey et al., 1982; Pirkle et al., 1994), in many impoverished communities, large numbers of children who live in older, deteriorating housing continue to have elevated blood lead concentrations (Brown et al., 2000; CDC, 1991, 2001; LaFlash et al., 2000; Litaker et al., 2000). In addition to efforts to remove lead from the environment, preventive strategies have also been instituted at the individual level. Nutritional interventions are a possible means of reducing lead absorption and/or susceptibility, because lead is absorbed primarily from the gastrointestinal tract (Garber and Wei, 1974).

The goal of the current investigation is to determine the relationship between infant dietary intakes of protein, iron, zinc, calcium, vitamin D, and fat with lead levels among infants at 6 and 12 months of age. This study is distinguished by both the availability of longitudinal data on the lead levels and diets of very young children and the opportunity to analyze multiple nutrients.

2. Materials and methods

2.1. Albany pregnancy infancy lead study (APILS)

APILS is a prospective longitudinal study examining changes in lead levels through pregnancy, possible nutrient–lead interactions, and the effect of a lead burden during the early postnatal period on infant growth and development. The study was conducted in two phases, the first from 1986 to 1992 and the second from 1992 to 1998. The first and second phases differed in follow-up protocol and lead measurement methods, and have been described elsewhere (Schell et al., 1997, 2000). This article presents findings generated from data collected in the second phase. All participating women gave their informed consent before data collection. The Institutional Review Boards of the New York State Department of Health, Albany Medical Center (AMC), and the State University of New York at Albany reviewed and approved all data collection methods and procedures for each phase.

2.2. Data collection and sample recruitment

APILS participants are some of Albany County's most socioeconomically disadvantaged pregnant women, drawn from a population that is at risk for lead exposure because of both their poverty and their residence in an urban center characterized by old, dilapidated housing adjacent to vehicular and industrial emissions. Women receiving first-time prenatal care at either the Albany County Department of Health (ACDH) Clinic or the AMC Obstetrics Clinic were invited to participate in the study. Participants were scheduled for one study visit during each trimester, including the trimester of enrollment. To be eligible for the study, each participant had to be a current resident of Albany county, be less than 24 weeks pregnant, receive prenatal care at ACDH or AMC clinics for at least two trimesters of their pregnancy, meet the eligibility requirements for the Women, Infants and Children program (WIC; $<185\%$ of poverty level), intend to deliver her infant at AMC and also receive subsequent pediatric care at ACDH or AMC, and allow a cord blood sample to be collected at delivery. Women were not eligible to participate in the study if their pregnancy was not a singleton pregnancy, if their pregnancies were considered high risk (women with high-risk pregnancies were referred for specialized care), if they were unable to complete all interviews in English (English fluency was necessary to meet other study goals that included standardized assessment of maternal cognitive performance), or if they already had a child in the study. The sample used in this study represents all the participants recruited into the study between September 1992 and October 1998, when recruitment was completed.

2.3. Blood sampling and analysis

The child's blood was drawn by a trained phlebotomist using a lead-free venous blood collection kit at delivery (cord blood 92%, venous 8%; 3 mL), at the 6-month pediatric clinic visit (16 mL), and again at 12 months (16 mL). All blood lead measurements were carried out in the Wadsworth Center's Lead Poisoning/Trace Elements Laboratory, using a Perkin Elmer (Norwalk, CT) Model 4100ZL atomic absorption spectrometer equipped with a transversely heated electrothermal atomizer (THGA) with longitudinal Zeeman background correction. The analytical method for blood lead, which was developed by the Wadsworth Center Lead Poisoning/Trace Elements Laboratory specifically for THGA furnaces, has been fully validated and described in the literature (Parsons and Slavin, 1993) and was subsequently adopted by the National Committee for Clinical Laboratory Standards for use by clinical laboratories using similar instrumentation (NCCLS, 2001). The method detection limit is 1 μg/dL, and result reproducibility (i.e, within-run SD) is typically 0.26 at 8.7 μg/dL. Intermediate precision (i.e., between-run SD) is typically 0.1–0.3 μg/dL below 10 μg/dL. Method accuracy is traceable to Standard Reference Material 955a Lead in Blood (National Institute of Standards and Technology) and Certified Reference Material BCR 194–195 (Commission of the European Communities). The Wadsworth Center's Lead Poisoning/Trace Elements Laboratory operates the New York State Department of Health's Proficiency Testing (PT) program for blood lead, and is the Department's

reference laboratory for this test. Method performance is continually monitored through participation in external PT programs operated by the College of American Pathologists, Wisconsin State Laboratory of Hygiene and the Pennsylvania Department of Health, and in External Quality Assessment schemes for blood lead operated by the United Kingdom, Germany (University of Erlangen), Spain, and Quebec, Canada.

This method has a minimum reportable limit for lead of 1.0 μg/dL (SD = 0.25 μg/dL). Consequently, values from 0.1 to 0.9 μg/dL can for clinical purposes only be reported as <1 μg/dL. However, for statistical analysis, laboratory values were used as reported by the instrument, including those <1.0 μg/dL, rather than using an imputation or substitution method. The rates of detection for lead at birth, 6 months, and 12 months of age were 85.4%, 93.2%, and 98.5%, respectively, in the sample of 169 infants who were not breast-fed.

2.4. Measurement of child's diet

During each pediatric clinic visit at 3, 6, 9, and 12 months of age, the child's diet was assessed using 24-hour diet recall as reported by the mother or primary caregiver. This technique provides detailed information on dietary intake for a short time period. Nutritionist IV software (Version 2.0, Salem, OR) was used to compute the intake of 37 macronutrients, vitamins, and minerals. Because daily fluctuations in dietary intake occur, a single 24-h diet recall is not necessarily representative of an individual's actual average consumption (Gibson, 1990; Willett, 1998). To increase the stability of our nutrient intake estimates, we averaged the intake of each nutrient across two time periods: the average of 3- and 6-month intakes, and the average of 9- and 12-month intakes. Although we could have averaged all four intake estimates, this choice would have entailed combining observations throughout infancy and, thereby, losing any ability to locate periods of sensitivity of dietary effects on toxicant burden. Furthermore, variability in individual consumption is likely to be relatively low here, because within-person variation of most nutrients is lower among children than adults (Willett, 1998). This suggests that an average of two intakes would be sufficient to achieve greater stability of our estimate while permitting tests of changes in nutrient–toxicant relationships. Protein, fat, iron, zinc, calcium, and vitamin D intakes were assessed here in relation to lead levels at 6 and 12 months. Vitamin and mineral supplement use was assessed as present or absent at each interview. The specific mineral and vitamin content of supplements could not be determined because of the variety in use and respondents' lack of awareness of formulation or brand name. Fluoride supplement use was noted separately from other supplement use. Two measures of nutritional status, serum vitamin D (1,25-OH vitamin D) and serum ferritin, were measured at the 9- and 12-month clinic visits.

2.5. The sample

Of the 317 eligible women, 71 terminated their pregnancies, moved, transferred care to another facility, or discontinued study participation before giving birth. An additional 34 women discontinued participation by the 3-month postpartum visit. Of the 212 participants remaining at 3 months, 33 women who reported any breast-feeding were excluded from analysis, because variability in the nutrient content of breast milk made it difficult to calculate accurate dietary nutrient intakes for their infants. Ten additional women had an indeterminate breast-feeding status resulting from missing data and were thus excluded. The 6- and 12-month blood lead concentrations of breast-fed infants did not differ significantly from the sample of infants who were not breast-fed. From the sample of 169 infants not breast-fed, three subsamples were derived for data analysis based on the availability of lead measurements at birth, 6, and 12 months of age.

Sociodemographic characteristics of the 169 mothers not breast-feeding are described in Table 1. A third of the sample of mothers identified themselves as white, and two thirds identified themselves as black, Hispanic, or other. The mean age of women at the time of enrollment in the study was 23.4 years, and 20.7% of the sample were younger than 19 years of age. At the time of their pregnancies, 59% of mothers had completed ⩾12 years of education. However, many mothers were too young to have completed high school. Among mothers

Table 1
Characteristics of mothers of non-breast-fed children enrolled in APILS, phase 2 ($n = 169$)

Categorical variables	Categories	n	%
Current marital status	Single	145	85.8
	Married	24	14.2
Race/ethnicity	White	57	33.7
	Black	78	46.2
	Hispanic	22	13.0
	Other	12	7.1
Age	⩽18 years	35	20.7
	>18 years	134	79.3
Completed education	<12 years	69	40.8
	⩾12 years	100	59.2
Prenatal cigarette smoking[a]	0 cigarettes	86	50.9
	<10/day	61	36.1
	⩾10/day	22	13.0
Continuous variables		Mean	SD
Height (cm)		163.3	7.65
Number of pregnancies		3.3	2.33
Number of live births		1.3	1.60

[a] Average number of cigarettes smoked per day during pregnancy.

⩾19 years of age, 71% had completed at least 12 years of education. The majority (86%) of mothers in this sample were single at the time of their entrance into the study. One-quarter of women in the sample had not been pregnant before, with a median prior gravidity of three pregnancies. Nearly half of the women in the sample had not given birth previously, with a median parity of one live birth. Approximately half of the women in the sample smoked cigarettes during their pregnancy.

2.6. Statistical analysis

Blood lead concentrations are log-transformed as a result of a non-normal distribution. The distributions of all dietary variables were found to be normal (Kolmogorov-Smirnov Test, $P \geqslant 0.05$) and were not transformed. Multivariable models were created to determine the relationship between intakes of single nutrients and lead at 6 and 12 months and the rate of change in lead during that time period: (12-month lead−6-month lead)/number of days between 6- and 12-month blood draws. All multivariable models were corrected for kilocalorie consumption because of the likelihood that mothers would overestimate infant dietary intake (Horst et al., 1988). Thus, the relationships tested here were between lead and the density of individual nutrients unaffected by variation in total kilocalorie intake. All multivariable models also included the child's lead level at birth. Because lead levels in the first year of life are strongly associated with lead levels at birth, the child's blood lead level at birth was included in all multivariable models as a means of testing relationships between diet and its effects on lead levels since birth. Effects of maternal diet on neonates' blood lead levels have been reported previously (Schell et al., 2003). Additional covariates were chosen on the basis of significant correlations ($P<0.05$) with lead levels and/or dietary nutrients. Candidate covariates were mother's age, marital status, education index (EI; see later), race/ethnicity, parity, cigarette smoking during pregnancy, child's body mass index (BMI) at blood draw, age of introduction of solid foods, serum vitamin D, serum ferritin, and child's supplemental vitamins (not including fluoride). All calculations were done using SPSS, Version 11.5 (Chicago, IL). All P values reported here are from two-tailed (nondirectional) tests.

Of the 169 mothers in this sample, 20.7% (35) were younger than 19 years of age. Because of the close relationship between age and education among mothers younger than 19 years of age ($r = 0.717, P<0.001$, $n = 35$), we constructed an EI of age-appropriate education that is used in place of maternal education in multivariable regression models. For persons younger than 19, EI = (years of education + 6)/age, and expresses the degree to which they are below or ahead of the age-appropriate year of schooling up to the completion of high school. For persons ⩾19 years of age, presumably old enough to have completed high school, EI = (years of education + 6)/18 (the age by which a person should have completed high school, allowing for one extra year). The EI is independent of age ($r = 0.057$, $P = 0.464, n = 169$) but closely related to maternal education ($r = 0.882, P<0.001, n = 169$).

3. Results

Infant blood lead concentrations rose quickly during the first year of life in this sample (Table 2). At 6 months, the geometric mean blood lead concentration was 2.3 μg/dL, and none of the infants had a blood lead concentration >10 μg/dL. This is a significant elevation from lead level at birth ($t = -7.4, P<0.001$). By 12 months, the geometric mean blood lead concentration had increased to 5.1 μg/dL (a significant elevation above the 6-month level; $t = -14.2, P<0.001$), and 18.25% of the sample had elevated blood lead concentrations (⩾10 μg/dL). There was no difference in mean levels by ethnicity/race at 6 months ($t = -1.08, P = 0.283$), 12 months ($t = -1.52, P = 0.131$), or in the rate of

Table 2
Blood lead, BMI, and age at which food groups were introduced of non-breast-fed children ($n = 169$) in APILS, phase 2

	Mean	SD	Maximum	n
Blood lead level				
Birth (μg/dL)[a]	1.6	1.00	6.5	151
6 months (μg/dL)[a]	2.3	1.59	8.9	147
12 months (μg/dL)[a]	5.1	4.18	23.9	137
6–12 months[b] (μg/dL/day)	0.02	0.018	0.07	123
BMI (kg/m^2)				
Birth	13.4	1.89	27.0	169
6 months	17.6	1.69	22.2	150
12 months	17.8	1.70	24.5	142
Age of food introduction (months)				
Milk[c]	10.4	2.50	>12 months	146
Fruit	4.1	1.70	9.3	165
Vegetables[c]	4.9	1.88	>12 months	162
Cereal	3.0	1.57	8.5	166
Meat[c]	7.0	2.27	>12 months	153
Eggs[c]	8.4	2.97	>12 months	146
Any solid foods	3.0	1.50	8.5	167

[a] Geometric mean calculated.
[b] The rate of change of the natural log of lead levels from 6 to 12 months; positive values indicate increasing lead levels. Arithmetic mean calculated.
[c] A value of 13 months was substituted for those individuals who completed a 12-month interview but had not yet introduced a given food group.

change in lead levels from 6 to 12 months ($t = -0.98$, $P = 0.328$). The frequency of lead levels $\geqslant 10\,\mu g/dL$ did not differ by ethnicity/race at 6 or 12 months.

Mean, minimum, and maximum values for calcium, vitamin D, iron, zinc, protein, calories, and fat intakes are shown in Table 3. Individuals' dietary intakes of these nutrients are compared to Recommended Dietary Allowances (RDA; Subcommittee on the Tenth Edition of the RDAs, 1989) except for fat, which did not at that time have an RDA. In the first 6 months of life, few APILS infants were below the RDA for calcium, vitamin D, or iron, whereas 15.4% fell below the RDA for protein, 25% were below the RDA for calories, and 37.9% of the sample fell below the RDA for zinc. At 9 and 12 months of age, >20% of APILS infants were below the RDAs for calcium, vitamin D, iron, and zinc, and fully two-thirds of the sample was below standards for vitamin D intake.

Results of multivariable regression analyses are shown in Table 4. All models were corrected for kilocalories and neonatal lead level. The inclusion of additional covariates varied with the outcome variable: all analyses of lead at 6 months included parity, at 12 months all models included parity and EI, and all models for the rate of change from 6 to 12 months included parity, supplement use, and EI. The absence of a marker of ethnicity/race from most models is due to the similarity of black and white infants' mean lead levels throughout infancy.

The averaged intakes of calcium, protein, zinc, and iron at 3 and 6 months are negatively associated with lead levels at 6 months of age. At 12 months of age, blood lead levels are negatively associated with averaged 9- and 12-month iron intake and positively associated with averaged 9- and 12-month protein intake. The rate of change in lead levels from 6 to 12 months also is positively associated with protein intake and negatively associated with iron. Because other studies have found that lead levels can be associated with ethnicity/race, maternal age, and supplemental vitamin use (Brody et al., 1994; Lauwerys et al., 1983), we added these covariates to our models and observed that they changed β coefficients little and did not alter levels of statistical significance for any nutrient. In addition, we examined the roles of serum ferritin and serum vitamin D levels at 9 and 12 months to predict lead levels at 12

Table 3
Nutritional intakes of APILS children in comparison to the 1989 RDAs and percentage of participants below the RDA[a]

	Intake average				<RDA		RDA
	Mean	SD	Min	Max	*n*	%	
Calcium (mg)							
3 and 6 months	677.7	232.71	329.7	1567.5	6	3.6	400
9 and 12 months	865.0	400.63	267.8	3604.0	37	24.0	600
Vitamin D (mg)							
3 and 6 months	10.7	2.95	5.6	19.3	15	8.9	7.5
9 and 12 months	8.5	3.03	2.6	15.7	105	68.2	10
Iron (mg)							
3 and 6 months	16.7	6.56	0.8	44.9	2	1.2	6
9 and 12 months	16.9	10.99	0.5	107.6	31	20.1	10
Zinc (mg)							
3 and 6 months	5.7	1.55	3.1	10.2	64	37.9	5
9 and 12 months	6.2	1.99	1.3	13.3	40	26.0	5
Protein (g)							
3 and 6 months	18.2	5.81	9.1	39.1	26	15.4	13
9 and 12 months	36.0	14.44	9.2	86.3	5	3.2	14
Calories (kcal)							
3 and 6 months	802.1	213.7	409.0	1406.5	50	29.6	650
9 and 12 months	1154.9	340.47	251.0	2797.5	25	16.2	850
Fat (g)							
3 and 6 months	39.4	10.68	22.4	70.2			
9 and 12 months	46.3	15.63	10.7	114.0			

[a] The 3- and 6-month daily intake average (APILS, $n = 169$) was compared to the 0.0- to 0.5-year RDA. The 9- and 12-month daily intake average (APILS, $n = 154$) was compared to the 0.5- to 1.0-year RDA.

Table 4
Relationship of child's nutrient intakes to lead levels at 6 and 12 months, and the rate of change in lead levels from 6 to 12 months through multivariable analysis[a]

Lead[b]	Nutrient[c]	β	β SE	Std. β	t	P value	Additional covariates
6 months	Calcium	–0.002	0.000	–0.59	–4.38	<0.001	C P
($n = 104-130$)	Protein	–0.058	0.017	–0.54	–3.36	0.001	P
	Zinc	–0.262	0.087	–0.62	–3.01	0.003	P
	Iron	–0.029	0.012	–0.32	–2.47	0.015	C P R
	Vitamin D	–0.051	0.032	–0.23	–1.58	0.117	P
	Fat	–0.016	0.012	–0.27	–1.37	0.173	P
12 months ($n = 123$)	Calcium	0.000	0.000	0.07	0.77	0.441	E M P
	Protein	0.013	0.006	0.29	2.15	0.034	E P
	Zinc	–0.009	0.038	–0.03	–0.24	0.812	E P
	Iron	–0.014	0.007	–0.18	–2.07	0.041	E P
	Vitamin D	0.008	0.019	0.03	0.40	0.692	E P
	Fat	0.009	0.007	0.22	1.29	0.198	E P
6- to 12-month rate of change ($n = 109$)	Calcium	0.000	0.000	0.08	0.73	0.465	E M P V
	Protein	0.000	0.000	0.40	2.70	0.008	E P V
	Zinc	0.001	0.001	0.08	0.63	0.532	E P V
	Iron	–0.001	0.000	–0.20	–2.12	0.036	E P V
	Vitamin D	0.001	0.001	0.12	1.26	0.210	E P V
	Fat	0.000	0.000	0.31	1.68	0.095	E P

Abbreviations: C, mother's prenatal cigarette smoking (average number of cigarettes smoked per day); EI, education index; P, parity (nulliparous; 1+ live births); M, marital status (married; single); R, race/ethnicity (black; white); SE, standard error; Std., standardized; V, use of supplemental vitamins at the 3- or 6-month visit.

[a] All models control for kilocalories and neonatal lead, and as noted, other significant covariates, which were chosen on the basis of a significant correlation or t-test with lead level or nutrient.

[b] The 6- and 12-month lead levels are log-transformed.

[c] Nutrient intakes at 3 and 6 months were averaged and used in regression models with 6-month lead levels. Nutrient intakes at 9 and 12 months were averaged and used in regression models with 12-month lead levels and the rate of change of lead levels from 6 to 12 months.

months and the rate of change in lead level from 6 to 12 months. In all cases but one they were not significant predictors. However, in the model predicting the rate of change in lead from 6 to 12 months, fat was a significant predictor when 12-month serum vitamin D was included in the model.

To estimate the impact of changes in maternal intake of important micronutrients, we calculated the change in a child's 6- and 12-month lead level with changes in intake of iron, calcium, protein, and zinc, from 1 SD below the mean intake to 1 SD above it, using the model and sample described in Table 4. A 2-SD decrease in child's intake of iron, protein, calcium, or zinc is associated with an increase in blood lead concentration at 6 months of 0.91, 1.57, 1.73, or 1.82 μg/dL, respectively. These changes in intakes of iron, protein, calcium, and zinc are equivalent to changes of 37%, 66%, 73%, or 76% of the mean 6-month blood lead concentration, respectively. A 2-SD decrease in iron (from 24.4 to 7.9 mg) is associated with an increase in 12-month lead of 1.21 μg/dL (24% of the mean of lead at 12 months), whereas a 2-SD reduction in protein (from 52.1 to 22.8 mg) is associated with an increase in 12-month lead level of 1.94 μg/dL (38% of the mean of lead at 12 months).

4. Discussion

In this sample, lead levels show the typical incline during infancy: they were low at birth, averaging only 1.6 μg/dL, and by 6 and then 12 months of age reached 2.3 and 5.1 μg/dL, respectively. These levels in phase 2 of APILS (1992–1998) represent a considerable decrease compared with data from the pilot study (phase 1 of APILS, 1986–1992) with a very similar Albany population. Mean values of lead levels cannot be compared across these two datasets because of differences in assay sensitivity at lower lead levels. However, the percentage of infants with an elevated lead level ($\geqslant 10$ μg/dL) can be compared. During the pilot study, 9%, 14%, and 37% of infants had elevated lead levels at birth, 6, and 12 months, respectively (data from Czerwinski, 1998), whereas during phase 2 none of the infants had elevated lead levels at birth or 6 months, and 18% had elevated lead levels at 1 year of age.

As sources of lead exposure are minimized, attention has turned to other strategies to reduce lead absorption and/or toxicity, including dietary modification. However, measuring the impact of diet in humans is complicated by difficulty in measuring intake, leading to enlarged variation in the estimate of intake (Gibson,

1990; Willett, 1998). The 24-h dietary-recall method tends to produce unstable estimates of typical intake (Gibson, 1990). This instability is mitigated in the present study by averaging intakes across two independent assessments 3 months apart. Also, the use of a retrospective diet recall is susceptible to bias due to the reliance upon memory. Unlike 24-h diet recall among adults, there may be a tendency to overestimate the infant's intake (Horst et al., 1988). We cannot test this source of error, and although there is no evidence that this varies in a nonrandom manner among the study population, the likelihood of overestimation prompted us to correct for kilocalorie consumption in the analysis of individual intakes. Thus, the relationships that were assessed here were between lead and the density of individual nutrients rather than the raw intake value.

Despite the low levels of lead in the study infants, the measurement error inherent in current methods of dietary assessment, and the small percentage of infants with nutrient intakes below the RDA (according to Table 3), we observed relationships between infants' lead levels and the dietary intake of protein, iron, zinc, and calcium at some point during the first year of life, but not with vitamin D or fat. These results are strengthened by the longitudinal study design. We were able to observe that differences in intakes at one age related to lead levels later in life. We also examined the time-reversed condition to test the possibility that lead levels were influencing diet or were characteristic of infants before the measurement of nutrient intake. For example, we observed that none of the 9- and 12-month nutrient intakes were associated with lead level at 6 months, whereas 3- and 6-month intakes of iron, zinc, calcium, and protein were each associated with 6-month lead levels.

In the present analysis, calcium and zinc intakes shared the same pattern of relationship with infant lead levels. Lower levels of both calcium and zinc intakes were associated with higher 6-month lead levels, even when adjusting for covariates; no effect of either mineral was found at 12 months. An inverse association between dietary calcium and lead levels has been well documented in both laboratory animals (Barton et al., 1978a; Hsu et al., 1975; Mahaffey et al., 1973; Morrison et al., 1977; Six and Goyer, 1970) and humans (Blake and Mann, 1983; Heard and Chamberlain, 1982; Johnson and Tenuta, 1979; Mahaffey et al., 1986; Sargent et al., 1999; Sorrell et al., 1977; Ziegler et al., 1978). This interaction seems to stem from the tendency of lead to mimic calcium and to interfere with calcium-mediated cellular processes (Dave et al., 1993; Pounds, 1984; Pounds et al., 1991). A negative association between zinc and lead has been shown in experimental animal studies (Bushnell and Levin, 1983; el-Waseef and Hashim, 1985; Flora et al., 1989; Mahaffey, 1980; Petering, 1978). It is believed that dietary zinc can prevent tissue accumulation of lead by reducing the inhibitory effect of lead on certain enzymes involved in heme biosynthesis such as δ-aminolevulinic acid (Dutkiewicz et al., 1979; el-Waseef and Hashim, 1985; Flora et al., 1989; Haeger-Aronsen and Schutz, 1976). The lead-induced inhibition of enzymatic activity results in increased production in the blood of erythrocyte protoporphyrin, which is chelated by an abundant pool of free zinc, causing the observed rise in zinc protoporphyrin. Among the few human studies that have addressed the zinc–lead relationship, results have been mixed (Lauwerys et al., 1983; Thomasino et al., 1977).

We also found lower dietary iron intakes to be associated with higher blood lead levels—an effect that persisted through the first year of life. In experimental animal models, iron deficiency increased the absorption and toxicity of lead (Barton et al., 1978b; Hamilton, 1978; Ragan, 1977; Shukla et al., 1990; Six and Goyer, 1970). These results have been replicated in numerous human studies of children and adults (Hammad et al., 1996; Lanphear et al., 2002; Mahaffey and Annest, 1986; Markowitz et al., 1990; Szold, 1974; Watson et al., 1980, 1986; Wright et al., 1999; Yip et al., 1981; Yip and Dallman, 1984). The effects of lead on heme biosynthetic pathways are enhanced by low iron levels (Piomelli et al., 1987), and there is some suggestion that this may also be the case for the cognitive effects of lead (Wasserman et al., 1992).

In this study, protein was significantly correlated with all lead measures during the first year of life, even when adjusting for covariates. However, a negative association was observed at 6 months and a positive association at 12 months. Animal studies of effects of protein intake have also yielded conflicting results, with some finding positive associations (Conrad and Barton, 1978; Quarterman et al., 1978) and others demonstrating negative associations (Barltrop and Khoo, 1975; Flora et al., 1989; Mylorie et al., 1977). According to Quarterman et al. (1978), we would expect to find a positive association when measuring lead in the blood, as lead was measured in the present study. A negative association between protein and 6-month lead levels, as well as negative associations with zinc, iron, and calcium, may reflect greater sensitivity to nutrient deficiencies at this young age. The reversal in the direction of association between protein and lead from 6 to 12 months may reflect that, in this sample, protein intakes increased considerably from 6 to 12 months. At 12 months, only 3.2% of the study infants had protein intakes below the RDA, whereas at 6 months, four times as many had intakes below the RDA. Unfortunately, direct testing of the effect of not meeting the RDA for nutrients was impossible, because the percentage of infants with intakes below the RDA was too small except in the case of zinc, where 37.9% did not meet the RDA. No significant effect was found.

Several explanations for the shift in results concerning zinc and calcium from the first to the second half of infancy are possible on the basis of pattern of intakes characterizing the sample. First, we note that the percentage of infants not meeting the RDA for calcium in the second half of infancy was far greater than in the first half. It is possible that intakes in the second half of infancy were all so low that many infants became similarly susceptible to absorbing lead from their environment. In other words, differences in intake could have been insufficient across the physiological range of activity to produce variation in the outcome of lead level. A related possibility is that the dietary variables found to be protective in the first half of infancy are effective only in the presence of low exposure to lead in the environment. Typically, contact between the infant and the environment is much greater in the second half of infancy, and lead absorption is also greater during that period. Increased exposure in older infants could overwhelm the effects of dietary influences, especially when the diet is poor.

Another reason for the weaker relationships in older infants between calcium and zinc intakes and lead levels is an increase in the variance for each intake estimate. This increase can result from greater error in estimating intakes among the older infants. Younger infants' diets were based almost entirely on formula with little variation, such that they are probably more accurately characterized by two 24-h food recalls. Older infants' diets are more variable, probably as a result of the variable introduction of some solid foods around 6 months of age. This variability is borne out by the increased SDs at 12 months of age (Table 3). The SD for calcium intake is nearly 2 times greater and that for zinc is 1.3 times greater in the older infants. This suggests that characterization of the diets of older infants may require more observations than we were able to include.

In this study, we observed no association between lead and fat or vitamin D intake at 6 or 12 months of age. Of the nutrients considered in this article, these two have been studied the least and have yielded conflicting results. A positive relationship between lead and dietary fat has been demonstrated in humans and an animal model (Bell and Spickett, 1983; Gallicchio et al., 2002; Lucas et al., 1996). However, the relationship between dietary fat and lead absorption is complicated by variation in effect depending upon the amount and type of fat in the diet (Barltrop and Khoo, 1975; Ku et al., 1978; Quarterman et al., 1977). Animal studies have shown positive relationships between vitamin D intake and lead (Edelstein et al., 1984; Mykkanen and Wasserman, 1982; Smith et al., 1978). However, studies among humans have been unable to demonstrate a relationship between vitamin D intake and lead (Koo et al., 1991; Laraque et al., 1990).

A major strength of the present study is its emphasis on very young children. Until now, most studies of nutrition and lead levels have looked at human adults or animals. By using longitudinal data and correcting for lead levels at birth, we have been able to strengthen the argument for a causal relationship between infant diet and the infant's acquisition of lead.

Although a high percentage of the study participants were minority group members, were poor, and lived in an old city, this sample may not be representative of the US population that have these characteristics. The subjects self-selected by choosing to seek prenatal care in the first half of pregnancy and by agreeing to meet the additional eligibility requirements described in Section 2. Thus, the generalizability of these results to all high-risk populations should be viewed with some caution.

On the basis of these results and those from other investigations, public health policy makers should consider reexamining the RDAs for zinc, iron, and calcium from the perspective of reducing lead absorption by infants. Health care providers to families with infants should include more extensive dietary counseling to ensure that infants consume diets rich in zinc, iron, and calcium. When faced with treating lead-poisoned children, providers should strongly consider supplementing with iron, calcium, and zinc.

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